# Chlorfenapyr
# (PIRATE™ , ALERT™, AC 303,630)
# Insecticide-Miticide
# Environmental Fate and Ecological Effects Assessment and Characterization for a Section 3 for Use on Cotton

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## EXECUTIVE SUMMARY

This document presents the results of an Environmental Fate and Effects Division (EFED) assessment of risks of registration of chlorfenapyr for use on cotton to terrestrial and aquatic organisms. The risk assessment builds upon previous EFED risk assessments[1] for this combination of chemical and use site, but incorporates important changes in chlorfenapyr labeling, additional toxicological data (avian, aquatic, and benthic invertebrate), measured residue data in terrestrial wildlife food resources, and new exposure modeling approaches for both terrestrial and aquatic receptors.

The results of this risk assessment for uses of chlorfenapyr consistent with proposed labeling demonstrate the following:

- Terrestrial wildlife dietary residues present a substantial risk to avian species. Exposure levels for all application rates exceed the threshold for reproductive effects for all of the species selected to represent avian receptors in cotton fields. Terrestrial wildlife exposures above reproductive levels of concern extend for multiple weeks after initial chlorfenapyr application. All proposed application rates also result in dietary residues that pose acute lethal risks to birds for many days after treatment. Even when assumed exposures are reduced to levels below those expected for minimal avian use of cotton fields, risks to reproduction are still indicated. Timing of chlorfenapyr applications to the cotton crop coincide with the reproductive window of most of the more than 50 species of birds that the registrant reports to be associated with cotton fields.

- Chlorfenapyr applications to cotton present acute risks to freshwater fish and invertebrates in United States Department of Agriculture (USDA) agricultural census regions 4 (AL, GA, KY, NC, SC, TN, VA), 6 (AR, LA, MO, MS, OK), and 7 (TX). Chronic risks to freshwater fish and invertebrates are not expected. However, for estuarine and marine organisms, this risk assessment predicts acute

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[1]EFED risk assessment documents for chlorfenapyr use on cotton include: Ecological Risk Assessment Briefing Packet for Chlorfenapyr, May 1, 1997; Section 3 EFED Assessment (DP Barcode: 210808)

and chronic toxicological risks. Chronic risk quotients for marine invertebrates exceed the level of concern by over an order of magnitude.

- Acute risks to sediment-dwelling invertebrates are not evident for freshwater systems receiving cotton field runoff. Levels of concern for these organisms are not exceeded by modeled sediment residues. However, because the persistence of chlorfenapyr suggests that longer term exposures are possible, the lack of a chronic freshwater sediment toxicity test represents an important data gap.

- Preliminary Risk Quotients for sediment-dwelling marine amphipods suggest that acute high risk, restricted use, and endangered species LOCs are exceeded by factors ranging from 2.4 to 5.4 for aerial and ground applications in Regions 4, 6,7, and 11.

These risk assessment conclusions are consistent with the findings of previous risk assessments for chlorfenapyr use on cotton. However, the confidence of the present avian risk findings is greater than in previous assessments because of the following factors:

- use of measured residue values in seeds, insects, and forage

- assessment of risks to specific species known to occur in cotton fields, including species-specific considerations of life history information, dietary preferences, and metabolic requirements

- incorporation of information specific to the use of cotton fields as a food resource

Where appropriate, this risk assessment has utilized information presented in the registrant's ecological risk assessments for terrestrial (MRID 444779-01) and aquatic (444526-02) organisms. This information primarily related to aspects of exposure characterization.

This risk assessment represents a change to the EFED Risk Quotient approach in that it models terrestrial exposures for specific species known to occur in cotton fields on the basis of measured ("real") pesticide residues in dietary items and presents levels of exposure over time. For aquatic organisms, the registrant used the <u>Mu</u>ltiple <u>Sc</u>enario <u>R</u>isk <u>A</u>ssessment <u>T</u>ool (MUSCRAT) for exposure modeling. MUSCRAT is otherwise identical to the PRZM/EXAMS model (the current EFED standard), except that it is statistically weighted to take into account spatial and temporal variability between use sites within the cotton-growing regions of the United States. Since use of MUSCRAT is provisional in EFED, EFED has computed concentrations using both MUSCRAT and the PRZM/EXAMS standard cotton scenario. Results are comparable (see Aquatic Organism Exposure Assessment). Therefore, to provide a methodology consistent with that which the registrant used, on an *ad hoc* basis, EFED has selected MUSCRAT concentrations for aquatic risk assessment purposes. In addition to water column estimates, because of previous concerns for potential toxic risks to sediment-dwelling organisms, this risk assessment evaluates risks to these organisms from water bodies receiving pesticide runoff from cotton fields.

For assessing risks to avian and mammalian species, the approach considers dietary exposures only. The assessment does not quantify exposures associated with oral ingestion during preening, ingestion of pesticide via drinking water, dermal exposures due to contact with treated surfaces, inhalation of pesticide volatilized to air or associated with suspended particulate. The assessment uses the most sensitive avian toxicological endpoint as the toxicological threshold, regardless of species, without modification to account for potential interspecies differences in sensitivity. The avian and mammalian risk assessments do not factor in the impacts of local environmental conditions as they relate to the spacial and temporal distribution of pesticide residues in the field. By using an alternative method for estimating dietary exposures than normally used by EFED, this assessment does not account for a number of safety factors built into the normal EFED Risk Quotient approach.

## USE PROFILE

### Chemical Identification

The chemical name for the pesticide compound AC 303,630 Technical is (4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1H-pyrrole-3-carbonitrile). The common name for the compound, as it is referred to in this risk assessment, is chlorfenapyr.

### Type of Use

Chlorfenapyr is proposed for use as an insecticide and miticide.

**Use Site**

The proposed use site is cotton.

**Target Pests**

Mites, beet armyworm, tobacco budworm, and cotton bollworm are the target pests on cotton.

**Formulation Type**

Chlorfenapyr will be marketed as two formulas:

PIRATE™ (eastern United States market)
One gallon contains 3.0 lbs of active ingredient.
Active ingredient = 30.83%, Inert ingredients 69.17%.

ALERT™ (western United States market)
One gallon contains 2.0 lbs of active ingredient.
Active ingredient = 21.44%, Inert ingredients = 78.56%.

**Method, Rate, and Timing of Application**

The recommended application methods are ground spray and aerial spray. The maximum application rate for PIRATE use on cotton for a single cropping season is 0.5 lbs ai/acre. Table 1 is from the proposed label and outlines the target pests, application timing and range of application rates.

The registrant's avian risk assessment (MRID 444779-01) has identified the expected timing of chlorfenapyr applications:

Pirate Applications: All target pests on mid- to late-season cotton - potential application window extending from July through September

Alert Applications: Mite control on seedling cotton - potential application window extending from May to early June

All target pests on mid- to late-season cotton - potential application window extending from July through September

The proposed label for the Alert product contains language prohibiting more than two applications in a given year. However, the Pirate label contains no such language. (Note: for the purposes of this risk assessment, the number of applications modeled for exposure purposes reflects the maximum number at a given application rate that will not exceed the maximum application rate of 0.5 lb ai/A, these maximum numbers of applications are also presented in Table 1.)

## ENVIRONMENTAL FATE CHARACTERIZATION

### Preface

EFED previously completed full review and assessment of environmental fate studies for chlorfenapyr on 21 Oct 96. We concluded then that the fate data requirements to support the registration of chlorfenapyr on cotton, except for spray drift data and analytical methods validations, were satisfied.

The registrant, however, felt that the submitted studies reflected a persistence and an associated exposure that would not be realized under actual field conditions or, even if realized, would be inconsequential ecologically. They especially felt that the 3.8 year aerobic soil metabolism half-life which they had submitted (MRID 42770242) was anomalous, and that five field dissipation half-lives with individual statistical confidence intervals ranging from approximately one-half to two years more accurately represented the rate of degradation, even though there were major field study deficiencies, including no analysis for degradates. Chemicals with half-lives in this range are, however, still persistent. Testing the possibility of a lesser persistence, EFED accordingly presented terrestrial risk assessments covering a range of half-lives from one to 3.8 years. As was predictable from elementary principles, the results of the terrestrial assessments were largely insensitive to such long half-lives since so little degradation occurs within established ecological endpoint time frames. Of course, overall environmental contamination or build-up in environmental compartments (soil, water, sediment, etc.) is very sensitive to rate of degradation or half-life, and compounds with half-lives as long as chlorfenapyr's will build-up, as is discussed later in this assessment.

In view of the conclusions from EFED's previous risk characterization which strongly indicated potential adverse effects, especially to avian species, the registrant chose to conduct additional lab and field studies, most of them innovative and non-guideline, to provide measured or "real" residues on wildlife food items, to provide better estimates of persistence in soil, and to provide other data which have elements of a probabilistic nature to "better define chlorfenapyr's environmental fate and effects" (quotation from registrant MRID 44452603). With the submission of these new studies, the registrant has now clearly established:

1) a statistical range of aerobic soil half-lives for chlorfenapyr in five different soils varying from 0.7 to 1.1 years with an average value of 0.96 $\pm$ 0.18 year and a standard upper 90% confidence limit of 1.4 years. This was accomplished by repeating the initial laboratory aerobic soil metabolism study with the same soil, by testing four additional soils, by better control of experimental conditions, and through use of a reference (benchmark) compound. On this basis, the initial aerobic soil regression half-life of 3.8 years is anomalously long, and will not be used in any way for exposure assessment.

2) that much or most of the dissipation observed in the field is due to degradation.

In the process, they have also demonstrated that

1) because of chlorfenapyr's persistence, significant environmental build-up does occur; and

2) that concentrations on wildlife food items are similar to those used in EFED's previous risk assessments, and, consequently, do not significantly alter previous avian risk conclusions.

## Fate Summary and Conclusions

Agricultural Use Pattern

Chlorfenapyr is an insecticide-miticide intended for use on cotton (this action) and other crops such as citrus and vegetables (pending actions). The maximum annual use rate on cotton is 0.5 lb ai/acre. Additional use information is attached or incorporated in other sections of this document.

Persistence/Rate of Degradation

Chlorfenapyr's persistence is typified by a range of laboratory aerobic soil metabolism half-lives based on five soils of 0.7 to 1.1 years with an average value of 0.96 $\pm$ 0.18 year and a standard upper 90% confidence limit of 1.4 years (MRID 44452621). These results are exclusive of a previous, anomalous 3.8 year value (MRID 42770243). Its observed dissipation "half-lives" in five small-plot cotton field studies in four states ranged comparably from 0.48 to 1.1 years with an average value of 0.75 year $\pm$ 0.25 year with a standard upper 90% confidence limit of 1.3 years (MRID 43492850). Since there was no analysis for degradates in the five cited field studies, some of the observed field dissipation/dispersal may have resulted from off-plot transport, not degradation, effectively indicating a somewhat longer degradative half-life and prolonged concentrations in environmental compartments. Recent re-analysis of chromatograms (MRID 44452622) of soil samples recorded in these cotton field dissipation studies identified a small amount of AC 312094 as a metabolite, indicating qualitatively that at least some degradation had occurred. A recently submitted, radiolabeled, small-plot field study in cotton in North Carolina (MRID 44452623) systematically identified small amounts of several degradates (see Degradates below), consistent with those found in soil in lab studies, and detected the presence of other minor unknowns. Although there was unexplained loss of roughly 65% of radioactivity and irregular oscillations in the data during the North Carolina study (perhaps because of untested surface transport by rainfall away from designated subplot areas into plot fringes which were framed by wooden barriers), the ratio of recovered parent radioactivity to total radioactivity (parent plus transformation products) as a function of time provides a normalizing measure of degradation rate (half-life). However, this relationship is valid if, and only if, it is assumed that all recovered materials and all missing materials (after separation from the original deposition) experience proportionately the same physical dissipation processes and are proportionately exposed to the same microscopic soil phases and surfaces for chemical or biochemical reactions. Under these assumptions, the resultant field dissipation half-life (first-order regression of time versus the natural logarithm of the percentage of parent in total radioactive residues) in the North Carolina study is approximately 0.9 year, with an upper 90% statistical confidence bound of approximately 1.3 years. These values fall in virtually the same range as found in the other field studies and in the lab aerobic soil metabolism studies.

Chlorfenapyr was essentially stable to laboratory hydrolysis and anaerobic soil metabolism. Under aerobic aquatic conditions, the average value for half-life in two German sediment compartments was 0.6 $\pm$ 0.2 year with an upper 90% confidence limit of 1.1 years; in the aqueous compartment, concentrations were essentially too low for precise analysis. Based on limited data in one aqueous compartment, EFED selected an upper bound modeling half-life for the aqueous compartment of approximately 0.8 year.

Degradates

Because of the persistence of chlorfenapyr and the consequent low yields of soil degradates during relatively short periods of study, EFED has not focused much attention on the role of transformation products in the risk assessment and risk characterization. Identified products are structurally similar to parent. Found in soil in field or lab studies were AC 303267, AC 303268 (the proposed toxic transformation product attributed for chlorfenapyr biological activity), AC 312094, AC 322118, AC 322250, and AC 325195 (see attached figure 1 for chemical structures). (Some of these transformation products exhibit ecotoxicity, some do not, while others have not been tested. None have been systematically subjected to the full complement of guideline tests for ecotoxicity. Results of available toxicity tests are presented elsewhere in this document. Of course, any associated ecotoxicity effectively serves to extend the persistence of parent.) Concentrations of these transformation products, when detected, were typically a few percent each or less of the applied chlorfenapyr. Only AC 312094, the desbromo derivative, sometimes approached or slightly exceeded 10% of total applied. *Relative* concentrations of AC 312094 in the radiolabeled North Carolina study were in the maximum range of 10-16%; *relative* maximum AC 325195 concentrations in the same study averaged less than 10%. Soil photolysis, with AC 325195 as a characteristic degradate, therefore plays a small role in chlorfenapyr's degradation (laboratory soil photolysis half-life of approximately 0.4 year). In general, transformation products appear to approximate or exceed the persistence of parent. Laboratory photolysis in water produced a major photoisomer AC 357806 (50-70% of total residues); this isomer was never reported as a product in any other lab or field study. Neither mineralization (carbon dioxide evolution) nor volatilization were significant in laboratory studies, and were not monitored in the field. The proposed cotton field degradation pathways for chlorfenapyr are attached (figure 1).

Build-up in the Physical Environment

Because of its persistence, the uniform, annual use of chlorfenapyr in a given area would result in significant build-up in environmental compartments. Commensurate with their half-lives, all chemicals undergoing first-order degradation come within 3% of their maximum value after a period of time corresponding to five half-lives; after ten half-lives the approach is within 0.1% of the maximum value. The exact general relationship of build-up in the soil compartment after years of uniform use with no off-site transport is best illustrated by the attached graph of concentration vs. time for selected half-lives (figure 2).

More specifically, if we select chlorfenapyr's previously cited 1.4 years aerobic soil metabolism half-life (approximately the same as the 1.3 years for field dissipation), then, after years of uniform use, the calculated asymptotic first-order value approaches 2.5 times the annual application amount (1.5 leftover from previous applications plus 1.0 from the current year application). Using the average aerobic soil half-life of 0.96 year, rather than the upper 90% limit of 1.4 years, the asymptotic value becomes 2.0 times the annual amount (1.0 residual plus 1.0 current). [Although not defensible scientifically or in a regulatory sense, if the even less conservative average field dissipation half-life of 0.75 year is naively selected, the asymptotic value is 1.7 times the amount applied annually (0.7 residual plus 1.0 current).]

Two supplemental multiyear soil accumulation-dissipation studies lasting approximately 4 1/4 years (five seasons, each with three uniform applications) in small bare soil plots in Italy and the United Kingdom demonstrate the trend towards increasing concentrations over time (MRID 44453624 plus updated summary data and analysis, barcode D246661, no MRID assigned). The attached figure 3 from the registrant (barcode D246661) summarizes the observations. In both countries, measured first year soil concentrations were approximately 0.1 ppm. Near the end of the studies the maximum concentration in Italy was approximately 0.3 ppm; in England, 0.4 ppm. However, because of severe limitations in study protocol and the pronounced oscillations in the data, these numbers are of marginal value and should not be conveyed in an absolute sense.

Nevertheless, the data clearly show significant residual concentrations and the relative trend towards asymptotic increases in annual peak concentrations.  Within experimental limits based on *actual* recovery from field soil (approximately 55% when corrected for 84-88% lab procedural recovery), and inclusive of at least some off-plot transport, build-up is realized.  Commensurate with half-life, the results approximate theoretical expectations.

Mobility

Chlorfenapyr has a relatively high soil to water partitioning ratio which correlates well with soil organic carbon content.  The average laboratory batch equilibrium $K_{oc}$ (adsorption coefficient normalized for organic carbon) for four soils was about 12,000 mL/g.  On this basis little vertical movement in soil would be expected.  Confirming this expectation, leaching was not significant in field dissipation studies.

*Ground Water Assessment*

Even though persistent, chlorfenapyr's relatively high sorption coefficients and the low potential for leaching exhibited in field dissipation studies preclude it from significantly affecting groundwater.  Any projected, hypothetical concentrations in ground water would be below the threshold of EFED's current SCI-GROW groundwater screening model.

*Surface Water Assessment*

Chlorfenapyr is, however, subject to enter surface water via runoff water and eroding sediment. As is discussed in the aquatic risks section of this document, chlorfenapyr's projected aquatic concentrations in water and sediment, in relation to its established ecotoxicity, clearly indicate potential surface water and sediment effects.  In addition to the currently projected effects, potential chronic toxicity in sediment is an issue still to be resolved.  Other indirect, general indicators of potential bioavailability are:  parent and identified degradates are easily extracted in high yield from soil or sediment with simple organic solvents, and chlorfenapyr is dislodgeable from cotton foliage.

Based on the current Pesticide Root Zone Model (PRZM 3.1.1) for cotton culture and the Exposure Analysis Modeling System (EXAMS 2.97.5), with added statistical weight through use of the *provisional* Multiple Scenario Risk Assessment Tool (MUSCRAT) option (see attached ecological risk documentation), tier 2 estimates of peak drinking water concentrations in surface water sources in four representative census of agriculture regions ranged narrowly from approximately 2 to 5 parts per billion (ppb). The 90-day surface water concentrations ranged from approximately 1 to 2 ppb. Post-processing of MUSCRAT outputs beyond 90-days is not a current option.

Bioconcentration

Chlorfenapyr did not concentrate in bluegill sunfish. Instead, it was metabolized to AC 312094 which concentrated up to 2300 times in whole fish, but was depurated with a half-life of roughly 4 days (97% depuration after 21 days). It should be noted that the environmental persistence of chlorfenapyr may reduce the potential for biologically significant levels of depuration. In addition, because of its lipophilicity (octanol/water partitioning ratio of 68,000); the presence of chlorine, fluorine, and bromine atoms; and the previously mentioned potential bioavailability of parent and degradates in high yield from sediment, chlorfenapyr may concentrate in invertebrates such as mollusks which generally have lower capacity to detoxify and which could receive prolonged exposure in sediment. The former Assistant Administrator of the EPA ORD (Robert Huggett) offered an emphatic professional opinion that bioconcentration in invertebrates was an important concern. The potential for chlorfenapyr accumulation in the invertebrates, and the risks of accumulation of AC 312094 in fish with respect to aquatic organism-consuming wildlife have not been addressed in this risk assessment.

Analytic Limitations

Because of chlorfenapyr's very high ecotoxicity, currently reported analytical precision limits for its measurement in water (1 ppb for quantitation, 0.1 ppb for detection) need to be improved by a factor of five or ten in order to meet a criterion of detecting about one-tenth of the trace concentrations with observed ecological effects. In addition, depending on the outcome of a recommended chronic toxicity study, a more sensitive analytical method for sediment concentrations may be necessary. It is a concern that adequate analytical methods be available for all pesticidal chemicals. Otherwise, in the event of an adverse incident there can neither be freedom from implication nor attribution of cause.

## Field Residue Studies

Foliar, Insect, and Soil Residue Study

A single application of the chlorfenapyr was made to cotton fields (one plot at 0.2, one plot at 0.4 lbs ai/acre, and two untreated plots, MRID 434928-14). Residues reported on cotton leaf tissues five hours after the 0.4 lbs ai/acre application were 183% of residues predicted by Fletcher et al. (1994)[2]. By day 28 residues on cotton foliage were approximately 3 mg/kg. Residues were determined on live insects collected both within the treated field and in the adjacent field border. It should be noted that there is uncertainty over the collection of only live insects as it is possible that such collection methods may produce an underestimation of residues in insects, if those still alive after treatment have not have received a maximal dose of insecticide. No chlorfenapyr was detected in insects collected from the adjacent habitat. Residues in insects collected within the field averaged 5.7 mg/kg through day 2 and dropped to levels below the method detection limit between days 7 and 14. Seeds collected from weeds within the adjacent habitat had no detectable residues. Soil residues were 158 $\mu$g/kg immediately following application and peaked at 170 $\mu$g/kg on day 14. By day 28 residues in soil averaged 100 $\mu$g/kg. It was determined through foliar leaf testing that nearly all chlorfenapyr on foliage was easily removed with a mild surfactant and water solution, regardless of the sampling time.

Weed Seed/Seed Head Residue Study

MRID 444526-08 presents the results of a study of the dissipation of chlorfenapyr in the seeds and seed heads of weedy plant species. Performed on a sandy loam soil field site in Stoneville, Mississippi, the study involved the treatment of plots planted in mixed weed seeds with three treatments of 0, 0.35, 0.18, 0.035, or 0.0075 lb ai/A for total applications of 0, 1.0, 0.5, 0.1, and 0.03 lb ai/A, respectively. From control and treated plots (one per treatment and control), weed seed heads, and composite and individual weed seed samples were collected an analyzed for

[2]Fletcher, J.S., J.E. Nellesen, T.G. Pfleeger. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. Env. Toxicol. Chem. 13:1381-1391.

chlorfenapyr. The results for weed seed heads and weed seeds are summarized in Table 2. Day 0 application residues for weed seeds and seed heads from this study are actually higher than residues predicted by Fletcher et al. (1994) for pods and seeds (e.g., Fletcher et al.: 24.6 mg/kg for 1 lb ai/A X 0.35 lb ai/A= 8.61 mg/kg versus Day 0.1 weed seed head field data for 0.35 lb ai/A = 27.2 mg/kg) or fruits (15 mg/kg 1 lb ai/A X 0.35 lb ai/A= 5.25 mg/kg versus Day 0.1 weed seed head field data for 0.35 lb ai/A = 27.2 mg/kg). It should be noted that the majority of data points are for a single analysis of a single composite sample collected from the corresponding treatment plot for each time interval. In a few cases, multiple chemical analyses (usually a duplicate analysis) were conducted on a single composite sample. While duplicate chemical analyses may test for analytical procedure variability and homogeneity of sub-sampling, the use of a single composite sample does not allow for an assessment of field variability. Therefore confidence intervals for these data points cannot be determined.

Insect and Cotton Plant Residue Study

MRID 444642-01 presents the results of a study of residues in insects as a result of single applications of chlorfenapyr to a single cotton field site under field conditions. The objective of the study was to determine the level of residues of chlorfenapyr in or on insects immediately after application and up to 28 days later. The test system consisted of larvae and adults of beet armyworms from laboratory reared colonies free from insecticides. Two broadcast applications of chlorfenapyr (0.2 and 0.35 lb/ai/A) were made to plots of cotton containing larvae and caged adults. The plots were located in Pulaski County Georgia. The test site consisted of two untreated control plots and four plots treated with chlorfenapyr. Two of the treatment plots were used for larval sampling, and two were used for adult moth sampling. Each of the larval treatment plots were divided into 22 subplots (2.9 m X 3.0 m). Three subplots were sampled per sampling period, with the insect samples composited within each subplot. The larvae and adults were collected for residue analysis. Adult insects were collected from cage enclosures at 0.1, 6, 15, 21, and 28 days after application. Larvae were sampled from the field on the day of and day after application. However, because field introduced larvae dispersed or pupated shortly after application, subsequent analyses of larvae were performed on laboratory reared larvae not directly treated with chlorfenapyr, but introduced in the laboratory to cotton samples taken from the treated fields at 3, 4, 8, 15, 22, and 29 days after application. Cotton residues were also collected and analyzed for chlorfenapyr.

Table 3 presents the measured chlorfenapyr residue data for adult and larval beet armyworms exposed either in-field or fed cotton plants collected from treated fields. The data are highly variable with respect to time period and are not consistent with respect to residues versus application rate. The registrant presented regressions (third order) of larval residue versus day after treatment. At both treatment levels (0.20 and 0.35 lb ai/A) the significance levels for these regressions (P= 0.0045 and p= 0.0004) suggested that the time after treatment slope of the data trends were significantly different from 0. However, the high variability of the data resulted in very poor predictive utility for the regressions ($r^2$ = 0.414 and 0.526 for 0.20 and 0.35 lb ai/A, respectively). It should be remembered that larval army worms were first exposed in the treated fields, but did not remain feeding on treated cotton plants. After initial exposure, larval army worms, raised on a dietary mixture containing no cotton, were exposed for only 3 to 10 hours in the laboratory to cotton plants collected from treated fields. These larvae were not in continual contact with treated fields, nor were data collected to demonstrate that the cotton plants introduced to laboratory armyworms (raised on a non-cotton food source), were actually consumed at a rate similar to those encountered in the field. There exists a potential that the measured residues from this study may underestimate actual in-field chlorfenapyr residues because of the short exposure period and the potential that dietary exposure was reduced due to the laboratory larvae unfamiliarity with cotton as a food source. Because of the potential for underestimation of insect residues inherent in MRID 444642-01, EFED elected to use the maximum values for each time interval as reflected in Table 3.

The registrant (Ahmed 1998a)[3] has supplied supplemental information regarding the frequency distribution of invertebrate residue levels collected with 24 hours of a foliar spray application of pesticides (an organophosphate and an aryl heterocyclic compound). These supplemental data can serve as a check on how conservative the use of maximum armyworm residues is for the risk assessment. The 95th percentile value presented in this distribution is approximately 20 mg/kg per 1 lb/A application. This 20 mg/kg value, adjusted downward to a 0.35 lb/A application rate (20 mg/kg X 0.35 = 7 mg/kg), is greater than the maximum measured Day 1 value of 4.34 mg/kg for armyworms feeding on plants from a chlorfenapyr-treated field at 0.35 lb ai/A. Therefore, the use of the maximum armyworm residues from MRID 444642-01 for the purposes of this risk

[3]Ahmed, Z. 1998a. Memorandum (with attachments) from Zareen Ahmed, Product Registrations Manager, American Cyanamid to Ann Sibold, Registration Division, USEPA/OPP, May 5, 1998.

assessment does not represent a conservative assumption.

Table 4 summarizes the results of the cotton plant analyses. For the purposes of this risk assessment, these cotton plant values were incorporated into oral exposures to forage for small mammals. It should be noted that these values are in close agreement with values predicted by Fletcher et al. (1994). For example, the Fletcher value predicted for short grass at 0.2 lb ai/A would be 48 mg/kg for (240 mg/kg X 0.2 = 48 mg/kg) and the average value from the measured residues at Day 0.1 for 0.2 lb ai/A is 45.9 mg/kg). Therefore, use of cotton plant residues as a surrogate for other plants potentially consumed by small mammalian herbivores is reasonable.

## TOXICOLOGICAL CHARACTERIZATION

### Biological Mechanism of Action

Chlorfenapyr (AC 303630) is a pyrrole insecticide-miticide. The compound is a pro-insecticide, such that the biological activity is incumbent on activation to another chemical moiety. Oxidative removal of the N-ethoxymethyl group of chlorfenapyr by mixed function oxidases forms the compound identified as CL 303268. CL 303268 functions to uncouple oxidative phosphorylation at the mitochondria, resulting in disruption of production of ATP, cellular death, and ultimately organism mortality.

It should be noted that CL 303268 has been detected in tobacco budworm larvae exposed to chlorfenapyr (MRID 444779-01). However, all monitoring data for insect larvae supplied by the registrant, and used in exposure estimations for this risk assessment, reports only chlorfenapyr residues. Consequently, the potential contribution of toxic CL 303268 residues in biological media that make up wildlife diets is not included in this risk assessment.

### Toxicity to Terrestrial Animals

<u>Acute and Subacute Avian Toxicity</u>

An acute oral toxicity study using the technical grade of the active ingredient is required to establish the toxicity of a pesticide to birds. The preferred test species is either mallard (a waterfowl species) or northern bobwhite (an upland gamebird). Results of these tests are listed in Table 5.  The most sensitive single oral dose $LD_{50}$ is for the red-winged blackbird (2.21 mg/kg, $LD_{50}$ values expressed on a bodyweight-based dose), which will serve as the toxicological endpoint in avian single oral dose exposure risk calculations.

All deaths reported for the mallard and northern bobwhite occurred within the first 3 and 7 days, respectively.  All red-winged blackbird mortality occurred within the first two days following treatment.  The $LD_{50}$ values for red-winged blackbird, mallard and quail were 2.21, 8.3 and 34 mg/kg, respectively.

Clinical signs of intoxication common to all three species included whole body and wing beat convulsions, lethargy and loose green or chalky excreta.  In addition, dyspnea (labored breathing) and opisthotonos (head stretched over back) were reported for the mallard.  Lethargy was reported in the highest red-winged blackbird dose group.  Post-mortem exam showed no treatment related abnormalities other than firm pectoral muscles.

A reduction in body weight, as compared to the control animals, occurred in the northern bobwhite at dose levels above 32 mg/kg during the first 3 days of the study.  No body weight reduction was noted in the mallards or red-winged blackbirds.

A reduction in food consumption, as compared to the control animals, occurred in the northern bobwhite at dose levels above 16 mg/kg during the first 3 days of the study. A similar response was observed in the mallard at treatments higher than 4 mg/kg.

These results indicate that chlorfenapyr is very highly toxic to waterfowl and passerine species and highly toxic to upland gamebirds on an acute oral basis.   The guideline requirement (71-1) is fulfilled (MRID 427702-27 and 427702-28).

In addition to acute toxicity testing performed with the technical grade of the parent compound, acute testing was conducted with metabolites which are produced under normal environmental conditions.  Table 6 lists the results of those tests.

AC 303,268, a soil photolytic degradate, was shown to kill nearly as quickly as the parent compound and was more toxic to northern bobwhite.  Deaths prior to day 4 accounted for 88% of the total mortality observed in mallards and northern bobwhite.  Weight loss coincided with decreased food consumption at day 3 at treatment groups 40 mg/kg and higher in the mallard and at 25 mg/kg and higher in the northern bobwhite. Signs of intoxication common to both species included shallow rapid breathing, reduced reaction time, and loss of coordination. Necropsy showed small pale yellow spleens and stained vents.

AC 312,094, a soil degradate and biological metabolite, was shown to kill slower than the parent compound and exhibit fewer negative impacts on the survivors. It is practically non-toxic to the mallard. No mallards died from the treatment nor were changes in behavior, weight or food consumption reported. However, it is considered slightly toxic to northern bobwhite. It killed northern bobwhite slower than the parent (33% of total mortality occurred by day 6). Weight loss and decreased food consumption occurred in the highest treatment group (1200 mg/kg) on days 3 and 7. After 7 days the food consumption in the high treatment group increased to quantities higher than the controls, but weight remained lower until the end of the study. Immediate symptoms of intoxication included rapid ventilation, esophageal fibrillation and ataxia. Longer lasting effects included unsteadiness, piloerection, inactivity and yellow-green feces.

CL 303,267, a soil metabolite, was shown to be practically non-toxic to both the northern bobwhite and the mallard duck. In the bobwhite, no test substance related mortality, moribundity, or signs of intoxication were observed in any of the definitive test birds. However, there were decreases in the 2250 mg/kg test group, as compared to vehicle controls, for bodyweight (day 0 to day 7). Mean feed consumption was lower at all doses when compared to controls. Two birds in the 2250 mg/kg treatment showed signs of emaciation, breast muscle atrophy, and bile duct pathology. In mallards CL 303,267 produced no test related mortality, moribundity, signs of intoxication, body weight abnormality, feed consumption changes, or pathological abnormalities.

CL 325,195, a soil metabolite, was shown to be slightly toxic to the northern bobwhite, and practically non-toxic to the mallard duck. In the northern bobwhite, effects observed in addition to mortality included bodyweight reductions, compared with controls, were observed for both the 455 and 700 mg/kg dose groups. Mean feed consumption was lower than controls for treatment groups 192, 296, 455, and 700 mg/kg. Pathological abnormalities with dose-related frequency, were observed in the 455 and 700 mg/kg treatment groups, consisting of emaciation and changes in breast muscle tone. Exposure of CL 325,195 to mallards produced no test-related mortality, moribundity, or signs of intoxication.  Mean feed consumption was reduced from controls in the 292 and 1350 mg/kg dose groups.  There were no bodyweight abnormalities nor pathological observations for any dose group.

These results indicate the metabolite AC 312,094 is practically non-toxic to waterfowl and slightly toxic to upland gamebirds.  The metabolite AC 303,268 is moderately toxic to waterfowl and highly toxic to upland gamebirds.   CL 325,195, is slightly toxic to upland gamebirds and practically non-toxic to waterfowl.  CL 303,267 is practically non-toxic to upland gamebirds and waterfowl.

Two subacute dietary studies using the technical grade of the active ingredient are required to establish the toxicity of a pesticide to birds.  The preferred test species are mallard (a waterfowl species) and northern bobwhite (an upland gamebird).  Results of these tests as well as a test using the passerine red-winged blackbird are listed in Table 7.  The red-winged blackbird $LC_{50}$ of 10.75 mg/kg-diet will serve as the basis of the toxicological endpoint for subacute dietary exposure risk calculations (note: a conversion to daily oral dose units is described later in this section).

All deaths reported for the northern bobwhite and mallard occurred within the first 4 and 5 days, respectively, with $LC_{50}$ values of 132 and 8.6 mg/kg-diet, respectively.   Clinical signs of intoxication observed in the mallard included lethargy, dyspnea, loss of coordination, loss of righting reflex, circling backwards and unusual head posture.  Northern bobwhites exhibited no symptoms other than irregular excreta.  Complete remission of all symptoms was achieved in survivors of both species by the beginning of the third day.  Post-mortem exam showed no treatment related abnormalities in either species, other than green gizzards and enlarged gallbladders in mallards.  Body weight reduction, as compared to the control animals, was noted throughout the entire study in the mallard at dose levels above 4 mg/kg-diet and northern bobwhite at dose levels above 80 mg/kg-diet.  Food consumption measurements showed only slight decreases at the two highest dose levels, as compared to the controls, for both species.  Measurements taken after day 2 showed no difference.

All birds found dead in aviaries for the red-winged blackbird test ($LC_{50}$ 10.75 mg/kg-diet) exhibited tetanus-like full-body rigidity.  No bodyweight changes nor food consumption alterations, with respect to controls, were observed for any treatment group.  The red-winged blackbird study incorporated two treatment groups at 14 mg/kg-diet to evaluate the effects of exposure timing on mortality. The standard treatment group were exposure through the diet for a total of five days. The satellite treatment group received treated diet for only the first 3 of 5 days. The satellite treatment birds exhibited no mortality, whereas the standard treatment birds exhibited all mortality on or before 3 days of exposure. No explanation for the differences between the onset of mortality for the standard and satellite treatment groups has been developed.

These results indicate that chlorfenapyr is very highly toxic to waterfowl and passerine species and highly toxic to upland gamebirds on an acute dietary basis. The guideline requirement (71-2) is fulfilled (MRID 427702-29 and 427702-30).

For the purpose of this risk assessment, the red-winged blackbird $LC_{50}$ was selected as the subacute dietary toxicity threshold. This selection is based on the selection of six passerine bird species as surrogate species representative of the birds observed to use cotton fields (as summarized in the avian risk assessment prepared by the registrant, MRID 444779-01). According to the tabular presentation in the avian risk assessment prepared by the registrant, the $LC_{50}$ for red-winged blackbird (expressed in terms of mg/kg-diet) was compared directly to avian dietary concentrations (a weighted average concentration expressed in term of mg/kg-diet). This approach does not account for the potential for varying food ingestion rates as a function of bodyweight. From the allometric equations incorporated in the registrant's avian risk assessment, it is evident that the proportion of bodyweight consumed as diet is not linear with respect to the bodyweight of the bird. Smaller birds consume more food per unit bodyweight than larger birds. Therefore, for a species-specific risk assessment, dietary exposures and dietary toxicological study endpoints should be expressed in terms of a daily dose in terms of mg/kg-body weight (mg/kg-bw/d). Expressing endpoints and dietary exposures in such terms accounts for the effect of ingestion rate on daily exposure. Note: this approach does not account for differing sensitivity to toxicants resulting from potentially different metabolic activation rates. The interspecies sensitivity may vary by as much as a factor of 10.

Expressing the red-winged blackbird $LC_{50}$ in terms of a subacute oral dose is accomplished by multiplying the endpoint by the average daily food intake for the closest treatment rate (in this case the 10 mg/kg-diet treatment group for the study consumed an average of 0.00993 kg per bird per day) and dividing the product by the average bodyweight (the 10 mg/kg-diet for treatment group's average bodyweight was 0.0653 kg). The result of this conversion is a subacute lethal dose (50% of the population) of 1.63 mg/kg-bw/d. It should be noted that the measurement of daily dietary consumption during many laboratory dietary studies is a crude estimate and may not fully account for a number of study-specific events that may contribute to uncertainty in the measurement.

The red-winged blackbird endpoint is not the most sensitive when expressed as a dietary concentration (the mallard LC50 is 8.6 mg/kg-diet versus the red-winged blackbird of 10.75 mg/kg- diet). However, when expressed in terms of a daily oral dose, the red-winged blackbird endpoint is more sensitive (1.63 mg/kg-bw/d for the red-winged blackbird versus 2.38 mg/kg-bw/d for the mallard).

Chronic Avian Toxicity

Avian reproduction studies using the technical grade of the active ingredient are required when any **one** of the following conditions are met: (1) birds may be subject to repeated or continuous exposure to the pesticide, especially preceding or during the breeding season; (2) the pesticide is stable in the environment to the extent that potentially toxic amounts may persist in animal feed; (3) the pesticide is stored or accumulated in plant or animal tissues; and/or (4) information derived from mammalian reproduction studies indicates reproduction in terrestrial vertebrates may be adversely affected by the anticipated use of the product. The preferred test species are mallard and northern bobwhite. Avian reproduction studies were required for technical chlorfenapyr for the following reasons.

> 1) The proposed labeling and usage of both PIRATE™ and ALERT™ allow multiple applications during a growing season, totaling no more than 0.5 pound active ingredient per acre per year. Some products can be applied to control early season pests, which coincide with breeding season.
>
> 2) Chlorfenapyr is slowly degraded under both aerobic and anaerobic laboratory conditions with a first-order half-life on the order of one or more years.
>
> 3) There exist data demonstrating chlorfenapyr residues in avian food items, including weed seeds, insects, and by analogy to cotton plant residues, forage.

The results of avian chronic tests are listed in Table 8. The mallard duck reproduction NOEL of 0.5 mg/kg-diet serves as the reproduction toxicity endpoint for avian long-term exposure risk calculations (note: a conversion to daily oral dose units is described later in this section).

Treatment-related differences were observed during the mallard experiment between the controls and treatment groups. In the 2.5 mg/kg-diet treatment group, reductions were observed for the total number of eggs laid, the number of viable embryos (immediately after laying), the number of viable embryos at 21 days of age (just prior to hatch), the number of normal hatchlings, the number hatchlings surviving 14 days, as well as a decrease in body weight of adult males. At a treatment level of 1.5 mg/kg a decline was noted in the body weight of the adult females. Food consumption declined with increasing active ingredient concentrations and was found significant in the 2.5 mg/kg-diet treatment group.

Reductions were observed in the number of northern bobwhite hatchlings surviving 14 days at a treatment level of 4.5 mg/kg-diet. Additionally, hatchling weight was lower at the 1.5 mg/kg treatment level.

The northern bobwhite study is determined to be supplemental and cannot be upgraded. However, the need for the new study is waived as the reported study has a very low NOEL, and a new study would not likely provide appreciably different results. Therefore guideline requirement (71-4) is fulfilled for the mallard (MRID 434928-13) but not the northern bobwhite (MRID 434928-11).

For the purposes of this risk assessment, the mallard chronic NOEL for reproduction was selected as the chronic avian endpoint. The avian risk assessment prepared by the registrant compared the NOEL for mallard (expressed in terms of mg/kg-diet) directly to avian dietary concentrations (a weighted average concentration expressed in term of mg/kg-diet). This approach does not account for the potential for varying food ingestion rates as a function of bodyweight. From the allometric equations incorporated in the registrant's avian risk assessment, it is evident that the proportion of bodyweight consumed as diet is inversely proportional to the bodyweight of the bird. Smaller birds consume more food per unit bodyweight than larger birds. Therefore, for a species-specific risk assessment, dietary concentrations and dietary toxicological study endpoints should be expressed in common units of a daily dose per unit bodyweight (mg/kg-bw/d). Expressing endpoints and dietary exposures in such terms accounts for the effect of ingestion rate on daily exposure.

Expressing the mallard NOEL in terms of a chronic oral dose is accomplished by multiplying the endpoint by the average daily food intake for the closest treatment rate (in this case the 0.5 mg/kg-diet treatment group for the study consumed an average of 0.1307 kg per day per bird) and dividing the product by the average bodyweight (the 0.5 mg/kg-diet for treatment group's average bodyweight was 1.106 kg). The result of this conversion is a chronic avian no observed effect dose of 0.059 mg/kg-bw/d.

Acute and Chronic Mammalian Toxicity

Wild mammal testing is required on a case-by-case basis, depending on the results of lower tier laboratory mammalian studies, intended use pattern and pertinent environmental fate characteristics. In most cases, rat or mouse toxicity values obtained from the Agency's Health Effects Division (HED) substitute for wild mammal testing. These toxicity values are reported in Table 9.

Acute exposure to technical chlorfenapyr in mice resulted in 95% of the deaths occurring within 24 hours at a dose level of 140 mg/kg with a combined (both sexes) $LD_{50}$ of 55 mg/kg. No important clinical or gross necropsy observations were reported.

On a unit of active ingredient basis, chlorfenapyr is more toxic as a formulated product. The combined species rat $LD_{50}$ for technical chlorfenapyr is 626 mg/kg. In contrast, the rat LD50 for the 2SC formulation (MRID 432682-04) is approximately 560 mg/kg and contains only 120 mg active ingredient. It is unknown if the increased toxicity is due to a additional substance in the formulation, a synergistic effect between the active ingredient and formulation ingredients, or variation between studies. Ultimately, the quantity of either formulation or the active ingredient to result in mortality is approximately the same.

Symptoms of exposure to AC 303,630 2SC include decreased activity, salivation, writhing and abnormal posture. Necropsy was unremarkable in surviving animals. In dead animals, grossly dark and mottled livers, pronounced striations of abdominal wall, tetany, salivation, pale intestinal tracts, dark lungs and diarrhea were observed.

Symptoms of exposure to AC 303,630 3SC in rats include decreased activity, salivation, ataxia, hyperthermia, protruding testes, prostration and death. Grossly congested and mottled livers and pronounced striations of abdominal muscles were observed at necropsy. Weight gains of the survivors were not affected.

The acute toxicity of four metabolites to rats was determined. Of those tested only AC 303,268 resulted in higher toxicity than the parent compound (e.g., combined sex $LD_{50}$s of 28.7 and 626 mg/kg for metabolite and parent, respectively). Of the 40 rats exposed to AC 303,268 at concentrations higher than 31.25 mg/kg, 39 died within 8 hours of dosing. Mortality occurred at a slower rate in tests with the other 3 metabolites but still most was observed within 3 days. Survivors of exposure to the metabolites exhibited no lasting clinical effects or notable findings during gross necropsy. No weight changes were reported for survivors. Clinical signs reported for exposure to the metabolites included decreased activity, prostration, ptosis, increased salivation and diuresis. Abnormalities found at necropsy included discolored livers and spleens, discolored and distended stomachs, and gas filled GI tracts. Striated muscle tissue was reported in animals killed by AC 303,268.

The sub-chronic LOEL (600 mg/kg-diet) and NOEL (300 mg/kg-diet) observed in rats (MRID No. 427702-19) are based on reduced body weight gain and increased relative liver weights in males, decreased percent hemoglobin and increased absolute/relative liver weights in females.

The sub-chronic LOEL (80 mg/kg-diet) and NOEL (40 mg/kg-diet) observed in mice (MRID 434928-30) is based on hepatic cell hypertrophy in $\leq$20% of test animal.

In a two generation reproduction study with rats (MRID 434928-36) the LOEL for systemic toxicity was 300 mg/kg-diet (22 mg/kg-bw/day) and based on pre-mating effects on parental weight gain. The LOEL for reproductive toxicity was 300 mg/kg-diet (22 mg/kg-bw/day) and based upon decreased lactational weight gains. The NOEL for these systemic and lactational weight endpoints was 60 mg/kg-diet. No effects were seen in reproductive performance parameters, other than those listed above, at any dose up to 600 mg/kg-diet (44 mg/kg-bw/day).

The results indicate that based on the most sensitive species, technical chlorfenapyr is highly toxic to small mammals (mouse $LD_{50}$ 55 mg/kg), AC 303,630 3SC is moderately toxic (male rat $LD_{50}$ 283 mg/kg), and AC 303,630 2SC is slightly toxic to small mammals (male rat $LD_{50}$ 560 mg/kg) on an acute oral basis. Male rats are 2.6X and 3.5X more sensitive than females when exposed to AC 303,630 Technical and AC 303,630 3SC, respectively. When exposed to AC 303,630 2SC and the metabolites AC 303,268 and AC 312,094, no differences were noted between sexes. Male mice are 1.7X more sensitive than females when exposed to technical chlorfenapyr. Males were roughly 2X more sensitive to the metabolite AC 325,195 than females, while the reverse was seen with AC 312,250.

Insect and Soil Organism Toxicity

A honey bee acute contact study using the technical grade of the active ingredient is required if the proposed use will result in honey bee exposure. A honey bee acute contact study is required for technical chlorfenapyr because multiple applications will be made throughout the growing season, including the period of flowering. Results of these tests are listed in Table 10.

The results indicate that technical chlorfenapyr is highly toxic to bees on an acute contact basis. However, no mortality occurred after the formulation is allowed to dry on vegetation, at application rates up to 0.43 lbs ai/acre. The guideline requirements (141-1) are fulfilled (MRID 427702-33 and 434928-45).

Two studies were submitted evaluating the toxicity of technical chlorfenapyr and AC 303,630 3SC on the earthworm *Eisenia fetida*. The results of these studies are listed in Table 11.

Earthworms in all treatment groups, including the control, lost weight in the acute toxicity study. Mortality was observed at treatment levels $\geq$17 mg/kg-soil. The 14-day $LC_{50}$ for survival was 22 mg/kg-soil. The NOEC for both survival and weight was 8.4 mg/kg-soil. No effect was observed on earthworm burrowing ability. Residue analysis was not conducted on earthworm tissue. A reference toxicant, 2-chloroacetamide, was used to validate the test methods. However, only 5% mortality was observed in the reference group instead of the expected 50%. The results of the reference treatment test indicate the experiment did not function properly and indicate that the actual toxicity of chlorfenapyr is higher than predicted.

No mortality was reported in the adults from sublethal exposure to AC 303,630 3SC at application rates up to 1.34 lbs ai/acre. Additionally, no differences were observed in either adult weight or the number of juveniles present at the end of the test. The positive control, benomyl produced significant ($p<0.05$) effects on earthworm weight, number of juveniles produced, and food consumption in accordance with a provision for clear sublethal effects as outlined in the testing protocol.

Terrestrial Field Testing

A terrestrial field test using the chlorfenapyr was requested by EEB on November 4, 1994, because the active ingredient is in a new class of pesticides (pyrroles) and has an entirely new mode of action (uncouples oxidative phosphorylation in the mitochondria). The field study request specifically stated methods in the Guidance Document for Conducting Terrestrial Field Studies (1988)[4], and recommendations of the Avian Effects Dialogue Group[5] be used in designing the field test.

The registrant has submitted the following five studies towards fulfilling this requirement (Table 12): a simulated field (pen) test and a dermal toxicity test with the northern bobwhite; an avian census of southern cotton fields and a field dissipation study of a single dose (0.2 lbs ai/acre) on cotton. In addition, the registrant has submitted two proposed study protocols. One protocol outlined methods to be used in an avian census study and another protocol detailed methods to be used in a habitat utilization study of red-winged blackbirds. Much of the information gained from the studies mentioned above can be used in this risk assessment. However, portions of some studies were rejected by EEB scientists due to unacceptable methods. None of the submitted studies meet the requirement of a field study.

**Simulated Field Pen Study.** Results from the simulated field (pen) study (MRID 438870-07 and 434928-14) indicate the active ingredient was not available to northern bobwhite. However, most of this study was invalid. One application was made to a cotton field at 0.35 lbs ai/acre. The high dose pen contained half treated cotton and half untreated field edge plants. The low dose pen was located in the plant zone bordering the treated field. The control pen was located in

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[4] Fite, E.C., L.W. Turner, N.J. Cook, and C. Stunkard. 1988. Guidance document for conducting terrestrial field studies. USEPA. EPA 540/09-88-109.

[5] Avian Effects Dialogue Group. 1989. Pesticides and Birds: Improving impact assessment. The Conservation Foundation.

untreated cotton. Test birds were de-beaked and provided clean feed *ad libitum*. One mortality occurred in the low dose pen and two in the high dose pen. Despite the observed mortality, most of this study was invalid for the following reasons: 1) birds were not placed in the pens until after the chemical had dried; 2) birds were provided clean feed during the entire study; 3) birds were debeaked prior to the experiment; 4) one-half of the high dose pen was located in habitat which received no direct pesticide application. An average of 83.7 mg/kg was reported on cotton foliage in the high dose treatment pens after one application. This value is 1.8X the concentration predicted by Fletcher (1995)[6]. Chlorfenapyr residues were not detected on the sorghum in the high dose pen after the first application, indicating little deposition on adjacent vegetation from drift. Sorghum in the low dose pens, 25 feet from the treated field, received little detectable active ingredient.

**Dermal Toxicity Study.** A primarily dermal toxicity study (MRID 438807-07 and 434928-14) with northern bobwhite was conducted to assess the risk of exposure through contact via exposed skin, such as the feet, through the feather layers and limited oral ingestion via preening. The 16 birds per treatment level were placed in 1.7 x 1.4 meter pens containing cotton treated at rates up to 4X the recommended application rate. The exposure period started after the chemical had dried. Following a 24 hour exposure period the birds were held for 27 days. Clean feed and water was provided *ad libitum*. No mortality or differences in body weight occurred in any treatment group. Residues on cotton leaf samples collected in the 1X treatment group were 0.8X the concentration predicted by Fletcher (1995). Maximum residues found on cotton leaf samples were about 320 mg/kg for after four applications at 0.35 lbs ai/acre. This study was not designed to assess the affects of exposure to the wet chemical.

**Avian Dietary Discrimination Study**. An avian dietary discrimination test (MRID 438870-07) was conducted with the northern bobwhite to determine the aversion qualities of chlorfenapyr. Technical material was mixed into a commercial diet at concentrations up to 250 mg/kg-diet and each bird (male, female, adult and juvenile) was presented with both treated and clean feed. Changes in body weight, consumption of treated feed and mortality were the measured endpoints. No mortality, weight change, or food consumption changes were noted in the adults in any

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[5] Fletcher, J.S. , J.E. Nellessen and T.G. Pfleeger. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. Environ. Toxicol. Chem. 13(9):1383-1391.

treatment group. However, five juveniles died at the 250 mg/kg-diet treatment level. Weight loss was reported in the juvenile treatment groups 250 mg/kg-diet by day 6; and in the 140 mg/kg for and 250 mg/kg-diet treatments by day 10. At the 250 mg/kg-diet treatment level, consumption of treated feed by juveniles was lower than the controls during the first 5 days of the test. It was reported that the northern bobwhite could not reliably discriminate feed treated with methiocarb, a known avian repellent, at concentrations less than or equal to 600 mg/kg-diet. The adult quail tested for aversion to chlorfenapyr did not alter their food consumption at concentrations up to 250 mg/kg-diet. Since 250 mg/kg-diet was the highest concentration tested it is not possible to determine if chlorfenapyr has similar repellency properties to adult quail as methiocarb. However, no deleterious effects were observed in the adults at the highest concentration. Juveniles on the other hand were notably impacted at concentration above 70 mg/kg.

**Avian Census (1993)**. A detailed census of the avian community in and around cotton fields was conducted in Arizona, Texas and Mississippi/Alabama, in 1993 (MRID 434928-14). EFED considers this study as a preliminary attempt to classify potential study locations in terms of vegetative type and structure, avian community structure, and avian use patterns to better design a future field study during which PIRATE will be applied. Approximately 175 surveys were conducted in each state. These were subdivided into plots representing riparian, agricultural and scrub/forest communities. Results of the surveys included the total number of individuals and species observed, most abundant species, avian community diversity, avian use of cotton fields and incidental wildlife observations. The five most common species observed during censuses are listed in Table 13.

Generalizing over all three regions, avian abundance was greatest in Arizona, nearly twice that of Mississippi/Alabama and more than twice that of Texas. Avian abundance and use of cotton fields increased as the growing season progressed. Time periods immediately prior to harvest had the greatest avian use. Forest and riparian habitats had the greatest avian abundance and diversity with the exception of Arizona study sites. Among all habitat types, upland forest sites in the southeast were the most diverse. Sites in Arizona adjacent to agricultural habitats had low avian diversity but high abundance due to high numbers of red-winged blackbirds. Species richness was highest in Arizona and Mississippi/Alabama

**Avian Census (1995)** In 1995, another detailed non-guideline avian census of cotton fields in Arizona, Texas, Mississippi, and Alabama was conducted (MRID 444642-02). Submitted to

EFED in January 1998, the study has been subjected to a preliminary review. The data from this study were incorporated only into the risk characterization portion of this risk assessment. Twelve cotton fields from Texas, twelve fields from Arizona, and twelve fields from Alabama and Mississippi were subjected to systematic field observation from June 8 to August 27, 1995. Avian censuses were taken during three separate periods between June and August and involved 8-minute visual observations taken three times per period for a total of nine 8-minute observation periods per cotton field. In addition, six 1-hour observation periods were conducted on each field for the purposes of surveying avian activity within the cotton fields.

A total of 54 bird species were identified as occurring in and around Arizona Fields; 47 species in Texas fields; and 54 species in Alabama and Mississippi fields. Of the total observations of birds in and around Arizona fields, 60% to 69% of the observations were for birds actually observed in cotton fields. In Texas, 21% to 27% of observations were for birds in fields. Approximately 11% to 24% of all observations for birds in and around Alabama and Mississippi fields were for birds actually within field borders.

**Study for Acute Effects (Carcass Searches and Radiotelemetry).** MRID 444526-16 presents the results of an avian telemetry/census and wildlife carcass search study of cotton fields treated with a single chlorfenapyr application 0.35 lb ai/A. This study was submitted to EFED in December 1997. This study was designed to evaluate acute effects in avian species from treatment of cotton fields with chlorfenapyr. This field study has not undergone a formal data evaluation at this time. It should be noted that past EFED recommendations for avian field testing have stressed the need to evaluate reproduction effects. The above study was not designed to measure such effects in the field.

Field Monitoring

MRID 438870-01 presents three reports summarizing wildlife mortality associated with single field applications of up to 0.2 lbs ai/acre. These monitoring efforts are of varying intensity and quality. However none were extensive enough to refute the risk to terrestrial wildlife. No dead or debilitated animals were found in any monitoring effort.

Mississippi State wildlife personnel conducted surveys in a total of 33 treated fields. The surveys included 70.3 acres of habitat adjacent to treated fields. No surveys were conducted within the treated fields.  Thirty-six percent of the surveys were conducted within the first 24 hours after application, 33% between 24 and 48 hours post-application, the remaining surveys were conducted 2,3, and 4 days post-application.  Twenty-six species were observed, of which 72% of all individuals were mourning dove, sparrows, cowbirds or red-winged blackbirds.

Alabama surveys were conducted by one individual and included 16 treated fields. The surveys encompass 20.4 miles of treated field (30%) and adjacent habitat (70%) transects.  One, two, and five surveys were conducted within 24 hours, 48 and 72 hours of treatment, respectively.  Twenty six species were observed within the treated field.  The four most common species within the fields were the indigo bunting, cardinal, red-winged blackbird and mourning dove.

Georgia State wildlife personnel conducted four surveys.  Elapsed time between treatment and surveys ranged from 3 to 15 days.  The author of the report stated no general conclusions should be drawn from the surveys regarding the effect of chlorfenapyr due to the excessive time between the application and survey.

**Toxicity to Aquatic Animals**

<u>Freshwater Fish Acute Toxicity</u>

Two freshwater fish toxicity studies using the technical grade of the active ingredient are required to establish the toxicity of a pesticide to freshwater fish.  One study should use a coldwater species (preferably the rainbow trout), and the other should use a warmwater species (preferably the bluegill sunfish).  In addition to these required tests, the registrant has also submitted a channel catfish (*Ictalurus punctatus)* study.  The results of these tests are listed in Table 14.

The results indicate that chlorfenapyr is very highly toxic to fish on an acute basis.  The guideline requirement (72-1) is fulfilled.

In addition, two freshwater fish toxicity tests were conducted on the major degradates.   The results of the major degrade, CL 312,094 (the desbromo derivative of the parent compound) is in Table 15.

The results indicate that the metabolite CL 312,094 $LC_{50}$ is greater than the highest test concentration. Consequently, the toxicity cannot be characterized for freshwater fish. However, since this degradate is less toxic than the parent compound, additional data will not be required at this time. The guideline requirement (72-1) is fulfilled for this degradate.

A rainbow trout acute toxicity test for CL 357,806, the degradate produced by photolysis in water, (MRID No. 438870-08) was classified invalid. A quantitative toxicity endpoint suitable for use by EFED in risk assessments could not be established for this study because of failure to measure the test concentrations as required. The data, if accurate, would suggest that this compound is more toxic than the parent and perhaps classify it as very highly toxic. Therefore, the guideline (72-1) is not fulfilled for this degradate. However, since photolysis in water is not expected to be a major fate pathway, the EEB is not requiring this study be repeated at this time.

Additionally, bluegill sunfish were tested with the soil metabolites CL 303,267 and CL 325,195. These tests were considered supplemental since chemical analyses were not performed and test concentrations were only measured at the initiation of the tests. The tests may be up-graded to core status if chemical characteristics such as solubility and adsorbing tendencies could be demonstrated. **However, until tests are upgraded to core status, the test results cannot be utilized in a risk assessment.** The purported $LC_{50}$s of the bluegill studies are less toxic than the parent. The results of the studies are presented in Tables 16 and 17.

Freshwater Fish Chronic Toxicity

Data from a fish early life-stage test using the technical grade of the active ingredient are required if the product is applied directly to water or expected to be transported to water from the intended use site, and when any **one** of the following conditions exist: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) any acute $LC_{50}$ or $EC_{50}$ is less than 1 mg/L; (3) the EEC in water is equal to or greater than 0.01 of any acute $EC_{50}$ or $LC_{50}$ value; or (4) the actual or estimated environmental concentration in water resulting from use is less than 0.01 of any acute $EC_{50}$ or $LC_{50}$ value and any one of the following conditions exist: studies of other organisms indicate the reproductive physiology of fish may be affected, physicochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g. half-life greater than 4 days). The preferred test species is rainbow trout. All the conditions stated above apply for chlorfenapyr except for condition (4). Results of this test are listed in Table 18. The results indicate that toxicological effects based on mortality first appeared at the 7.64 $\mu$g/L level. The guideline requirement (72-4) is fulfilled.

A fish life-cycle test using the technical grade of the active ingredient is required when an end-use product is intended to be applied directly to water or is expected to transport to water from the intended use site, and when any of the following conditions exist: (1) the EEC is equal to or greater than one-tenth of the NOEL in the fish early life-stage or invertebrate life-cycle test or; (2) studies of other organisms indicate the reproductive physiology of fish may be affected. The preferred test species is the fathead minnow. A fathead minnow study (MRID 443648-03) was reviewed and classified as Invalid because both control and solvent control appear to have been contaminated. Additionally, measured concentrations at all treatment levels were highly variable. This test must be repeated.

Freshwater Invertebrate Acute Toxicity

A freshwater aquatic invertebrate toxicity test using the technical grade of the active ingredient is required to assess the toxicity of a pesticide to freshwater invertebrates. The preferred test organism is *Daphnia magna*, but early instar amphipods, stoneflies, mayflies, or midges may also be used. Results of this test is listed in Table 19. The results indicate that chlorfenapyr is very highly toxic to aquatic invertebrates on an acute basis. The guideline requirement (72-2) is fulfilled.

In addition, a freshwater aquatic invertebrate test toxicity test was conducted on the major photolytic degradate in water, CL 357,806. The results of this study are listed in Table 20.

The results indicate that CL 357,806 is highly toxic to freshwater aquatic invertebrates. Since the $LC_{50}$ of 18 $\mu$g/L is less toxic than the parent compound additional testing will not be required for this degradate at this time. However, no data was submitted for the major degrade, CL 312,094 (the desbromo derivative of the parent compound), and the registrant does not explain the reason for the non-submission of data. Further acute testing for the desbromo compound will be considered after an explanation is submitted.

Acute tests for the soil metabolites CL 312,094, CL 325,195, and CL 303,267 were also submitted for the freshwater invertebrate *Daphnia magna*. These tests were considered supplemental since chemical analyses were not performed and test concentrations were only measured at the initiation of the tests. The tests may be up-graded to core status if chemical characteristics such as solubility and adsorbing tendencies could be demonstrated. **However, until tests are upgraded to core status, the test results cannot be utilized in a risk assessment.** The purported $LC_{50}$s for the bluegill are less toxic than the parent. The results are presented in the Tables 21 through 23.

Freshwater Invertebrate Chronic Toxicity

Data from an aquatic invertebrate life-cycle test using *Daphnia magna* are required if the product is applied directly to water or expected to be transported to water from the intended use site, and when any **one** of the following conditions exist: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) any acute $LC_{50}$ or $EC_{50}$ is less than 1 mg/L; or (3) the EEC in water is equal to or greater than 0.01 of any acute $EC_{50}$ or $LC_{50}$ value; or (4) the actual or estimated environmental concentration in water resulting from use is less than 0.01 of any acute $EC_{50}$ or $LC_{50}$ value and any of the following conditions exist: studies of other organisms indicate the reproductive physiology of invertebrates may be affected, physicochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g. half-life greater than 4 days). *Daphnia magna* is the preferred test species. All the conditions stated above apply for chlorfenapyr except for condition (4). Results of this test are listed in Table 24.

The results indicate that toxicological effects based on mortality first appeared at the 7.7 $\mu$g/L level. The guideline requirement (72-4) is fulfilled.

Estuarine and Marine Animal Acute Toxicity

Acute toxicity testing with estuarine and marine organisms (fish, shrimp and oyster embryo-larvae or shell deposition) using the technical grade of the active ingredient is required when an end-use product is intended for direct application to the marine/estuarine environment or is expected to reach this environment in significant concentrations. The preferred test organisms are the sheepshead minnow, mysid, and eastern oyster. Estuarine/marine acute toxicity testing is required for chlorfenapyr because the end-use product is expected to reach the marine/estuarine environment in significant concentrations. Results of these tests are listed in Table 25.

The results indicate that chlorfenapyr is very highly toxic to marine/estuarine organisms on an acute basis. The oyster shell deposition study (MRID 434928-17) was invalid due to inadequate growth in controls (< 2mm). Since an embryo-larvae study was not conducted, this study must be repeated. During the last submission of data (January 1998) neither a new shell deposition study nor an embryo-larvae study were submitted. The guideline requirement (72-3) still remains unfulfilled.

Estuarine and Marine Animal Chronic Toxicity

Data from estuarine/marine fish early life-stage and aquatic invertebrate life-cycle toxicity tests are required if the product is applied directly to the estuarine/marine environment or expected to be transported to this environment from the intended use site, and when any **one** of the following conditions exist: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) any acute $LC_{50}$ or $EC_{50}$ is less than 1 mg/L; (3) the EEC in water is equal to or greater than 0.01 of any acute $EC_{50}$ or $LC_{50}$ value; or (4) the actual or estimated environmental concentration in water resulting from use is less than 0.01 of any acute $EC_{50}$ or $LC_{50}$ value and any of the following conditions exist: studies of other organisms indicate the reproductive physiology of fish and/or invertebrates may be affected, physicochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g. half-life greater than 4 days). The preferred test organisms are the sheepshead minnow and mysid. All the conditions stated above apply for AC 303,630 except for condition (4). Results of this test are listed in Table 26.

The results indicate that toxicological effects based on mysid shrimp mortality first appeared at the 0.385 $\mu$g/L level. The chronic sheepshead minnow study (MRID 434928-20) was invalid due to low dissolved oxygen levels throughout the experiment. This study must be repeated. Therefore the guideline requirement (72-4) is not fulfilled.

An estuarine/marine fish life-cycle test using the technical grade of the active ingredient is required when an end-use product is intended to be applied directly to water or is expected to transport to water from the intended use site, and when any of the following conditions exist: (1) the EEC is equal to or greater than one-tenth of the NOEC in the fish early life-stage or invertebrate life-cycle test or; (2) studies of other organisms indicate the reproductive physiology of fish may be affected. The preferred test species is the sheepshead minnow.

An estuarine/marine study (MRID 443648-02) was reviewed and classified as Invalid because the control appears to have been contaminated. Additionally, mean measured concentrations were approximately 50% of nominal. Because the sensitivity of the analytical procedures ranged from 0.05 to 0.3$\mu$g/, it is possible that the solvent control contained as much as 2.7 $\mu$g/L chlorfenapyr. Therefore, this test must be repeated.

Aquatic Field Testing

Due to the aquatic concerns resulting from the use of chlorfenapyr the registrant submitted a microcosm study "to develop an understanding of the potential impact of the chemical on aquatic organisms under conditions more representative of an actual environmental application".

As explained in the abbreviated review, since EPA has no protocol or guidance documents for the review of microcosm studies, the results from this microcosm review can only be used as supplemental information. It was noted in the review that 90% and 100% mortalities for fish (bluegill sunfish) were observed at nominal concentration of 30 and 300 $\mu$g ai/L (11.33 and 221.32 $\mu$g ai/L measured concentrations), respectively.

Sediment Toxicity

To address the question of bioavailability of chlorfenapyr to benthic organisms sediment toxicity testing is required. At the time EPA requested this testing, the only protocol which had been fully developed was a 10-day acute sediment toxicity test. However, at this time EPA has developed a guideline protocol for a 28-day chronic sediment test. An acute sediment toxicity test for the freshwater amphipod *Hyallella azteca* was reviewed (MRID 444526-19). The results are presented in Table 27. The results indicate that mortality occurs to sediment dwelling organisms such as *Hyallela azteca* at a level of 19.6 mg/kg.

The marine amphipod has only just recently been submitted, and has not yet been subjected to a formal data evaluation by EFED. However, according to the results submitted by the registrant the measured 10-day acute $LC_{50}$ was 0.18 mg/Kg for the marine amphipod *Leptocheirus plumulosus***.**

**Toxicity to Plants**

Terrestrial Plant Toxicity

Currently, terrestrial plant testing is not required for pesticides other than herbicides, except on a case-by-case basis (e.g. labeling bears phytotoxicity warnings; incident data or literature which demonstrate phytotoxicity).

Aquatic Plant Toxicity

As with terrestrial plants, currently, aquatic plant testing is not required for insecticides or other classes of pesticides, except on a case-by-case basis (e.g. labeling bears phytotoxicity warnings; incident data or literature which demonstrate phytotoxicity).

## EXPOSURE ASSESSMENT

### Terrestrial Avian and Mammalian Exposure Assessment

Exposure estimates for avian and mammalian organisms in previous risk assessments for chlorfenapyr on cotton have been based either on the EFED approach using the Kenega nomograph (as modified by Fletcher et al., 1994)[7], or on an exposure estimation method founded on the assumptions of ubiquity and stability of chlorfenapyr and the use of predicted soil residues as a surrogate for other exposure media[8].

The subsequent availability of measured chlorfenapyr residues in avian and mammalian food items prompted the registrant to prepare an avian risk assessment incorporating such data for exposure estimating purposes. For this risk assessment EFED has elected to include these same residue data into the exposure assessment. This risk assessment incorporates such data in estimating avian and mammalian dietary exposures. Because the time periods for collection of samples for different avian food item residue studies were not completely consistent across all studies (e.g., weed seed head samples were collected on days 1,3, 15 after initial application whereas insect larval samples were not collected on these days) it became necessary, for

[7] Section 3 EFED Assessment (DP Barcode: 210808)

[8]Ecological Risk Assessment Briefing Packet for Chlorfenapyr, May 1, 1997

exposure modeling purposes, to include  a subset of residue data points in common to all studies.

The assessment does not quantify exposures associated with oral ingestion during preening, ingestion of pesticide via drinking water, dermal exposures due to contact with treated surfaces, inhalation of pesticide volatilized to air or associated with suspended particulate.  Because the available residue data are limited to studies of a few cotton fields, the avian and mammalian risk assessments do not factor in the impacts of  local environmental conditions as they relate to the spacial and temporal distribution of pesticide residues in the field.

**Residues in Dietary Items Adjusted to Label Conditions**

The registrant has submitted a variety of studies that present post application concentrations of chlorfenapyr in cotton plants, weed seeds, weed seed heads, and insects.  Brief synopses of the studies used in this EEC estimation approach are described in the environmental fate section of this document.  The residue data selected as the basis for estimating avian and mammalian exposures are from MRID 444526-08 and MRID 444642-01.

<u>Weed Seed Head Residues</u>

Table 2 presents the data for weed seed heads and weed seeds from MRID 444526-08.  The weed seed head data for each combination of treatment and sampling interval represents the results of a single composite sample.  The measured values for weed seeds represent primarily the results of single sample analyses, but at times are the results of averages of multiple analyses of the same sample.  A brief comparison of the composite weed seed head samples and the average concentrations of chlorfenapyr on weed seeds suggests that the two sets of data are roughly equivalent.  Therefore, the more extensive data set on weed seed heads was selected as the basis for estimating concentrations of chlorfenapyr residues for in-field seeds in the avian and mammalian diet.  EFED has used these data in this current risk assessment with reservation. The assessment results based on these data likely do not represent maximal potential residues in weed seeds or heads and, by extension maximal exposure levels for organisms feeding of weed seeds. By collecting composite samples across the plots, any variability associated with the spacial distribution of chlorfenapyr residues across the fields is lost.  It is not known how high maximal residues levels were in the treated plots.  Furthermore, data from a single field are not representative of environmental conditions for cotton fields across the cotton-growing portions of the United States.

Because the field study generating these data was conducted prior to the revised label rates, the application rates used in the study do not exactly match the new proposed label rate. To address the problem of non-matching application rates, weed seed head residues for tested application rates similar to the label rates were assigned to label rates as surrogate residues. It should be noted that the measured residues are likely underestimates of maximum possible residues because the treatment interval employed in the field was 7 days while a 5-day treatment interval is allowable under the proposed label. In addition, the use of composite samples in the available data does not address the potential for avian exposures as a result of feeding in localized areas of high residues as a result of non-uniform application. Table 28 presents estimated weed seed head residues for each application strategy allowed for on the proposed label. To estimate weed seed head residues at label rates, residue values for the closest tested application rate were multiplied by the ratio of label application rate to tested application rate (e.g., residues for a 0.2 lb ai/A application rate were estimated by multiplying the 0.18 lb ai/A application rate measured residues by the ratio of 0.2/0.18). Residue data from MRID 444526-08 were limited for each pest control application scenario to the actual number of applications allowed per year under the proposed label.

With respect to the output in Table 2, the rationale for estimating residues for shorter time periods for the 0.2, 0.25, and 0.35 lb ai/A application scenarios is as follows. Because the data from MRID 444526-08 involved three consecutive applications of chlorfenapyr, the full set of residue data cannot be directly applied to label application scenarios with less than three applications. If one used data following the last one or two applications, there would be overestimations of the residues in weed seeds that would not be consistent with label limitations. Therefore, although the MRID 444526-08 data set extends for all application rates to 56 days after first application, the residues for applications at 0.2, 0.25, and 0.35 lb ai/A were limited to only the sampling periods encompassed by either the first or second applications.

Because no residue studies for the fruits of wildlife-used plants have been submitted to the Agency, weed seed head residue data were used as a surrogate for fruits. The avian risk assessment prepared by the registrant (MRID 444779-01) used European study residue data for commercial fruit crops as a surrogate for fruits in wildlife fruits. EFED elected not to use this approach because these studies have not been submitted to the Agency, and the types of fruits used in the registrant's risk assessment included such items as tomatoes, which are not likely to be representative of the very small wild plant fruits likely to be encountered by wildlife.

Insect Residues

For the purposes of this risk assessment, data on the residues of chlorfenapyr in armyworm larvae (MRID 444642-01) were used to represent in-field insect residues potentially available to terrestrial birds and mammals feeding in cotton fields. The larvae were selected over the adult moths, as it is the occurrence of egg masses and hatching larvae that would trigger the application of chlorfenapyr and therefore offer the most probable route of exposure to avian species feeding on insects from the cotton fields.

Because the chlorfenapyr application rates employed in the beet armyworm residue study do not reflect the application rates allowed for by the proposed label, EFED adjusted the insect residues to account for these differences by multiplying the residue levels by the ratio of label application rate to test application rate. This adjustment conservatively assumes a linear relationship between application rate and insect residue level. The conservatism associated with this assumption comes from the observation in MRID 444642-01 that higher application levels do not necessarily result in higher insect residues. The registrant has postulated that once an insect lethal oral dose is achieved, the insects reduce or stop feeding. Because the armyworm larva study only presents data for a single application, a method for accounting for the effect of multiple application scenarios on insect residues was developed. The method essentially added residues from each subsequent application at a discrete time period. For example, with a seven day application interval, insect residues at 7.1 days after the first application were calculated as the residue value for a single application at 7 days post-treatment plus the residue for a second application as estimated from the 0.1 day residue for a single application. For the purposes of this risk assessment, a 7-day application interval was selected to remain consistent with the weed seed head residue data. It should be noted that the label allows for a 5-day application interval, so the residue estimates used in this risk assessment do not reflect a worst-case estimate. For the purpose of simplifying presentation and analysis, residue data estimates were limited to a time period of 0.1 to 28.1 days after the first application. Table 29 summarizes these results.

Cotton Residues as Surrogate for Forage

While residues have been measured in weed seeds, there are no data for residues in other portions of weed and grasses that could potentially be used as dietary items for small herbivorous mammals. Data from MRID 444642-01 presents the most complete data set for residues of chlorfenapyr on cotton plants. While cotton plants themselves may not be a principal source of vegetative forage for small mammals, the residue data for cotton is very close to concentrations of chlorfenapyr predicted by the standard EFED approach on short-grass forage, that would otherwise serve as the basis for residue-based exposure estimates. Therefore, these cotton data were used as a surrogate for forage plants. Table 30 presents chlorfenapyr forage residues, corrected for label application rates and number of applications. The data have been limited to a 28-day window to be consistent with other time-limited dietary item predictions.

**Soil Residues**

Soil residues were estimated on the basis of application rate for a 0-3 cm depth interval. A 3 cm depth was assumed to be the likely maximum depth of soil available for incidental ingestion by avian species using cotton fields. Chlorfenapyr concentrations in soil were calculated for each application scenario, using a multiple application interval of 7 days to be consistent with the interval employed in field/laboratory residue studies for avian food items. Because of the temporal limitation of the avian food item residue data (discussed below), soil residues were estimated to a maximum of 28 days following first application, and incorporated a 90 percent upper confidence limit half-life of 496 days. It should be noted that the proposed label allows for 5-day application intervals. The use of a 7-day interval in this risk assessment represents a less than worst-case scenario, although the long half-life employed in calculating soil residues suggests that the application interval difference would not greatly affect soil residue estimates. Table 31 presents the results of soil residue estimates.